AR 201-12549 b31

ROBUST SUMMARY
ALKYL SULFIDE CATETGORY
CAS # 67124-09-8
HEALTH ELEMENTS: REPEATED DOSE TOXICITY

Test Substance	
CAS #	CAS# 67124-09-8
Chemical Name	2-propanol, 1-(tert-dodecylthio)-
Remarks	100% purity This chemical is also referred to as propanol/dodecylthio derivative in the HERTG's Test Plan for Alkyl Sulfide Category. For more information on the chemical, see Section 2.0 "Chemical Description of Alkyl Sulfide Category" in HERTG's Test Plan for Alkyl Sulfide Category.
Method	
Method/Guideline followed	OECD 407
Test Type	28-day oral toxicity study in rats
GLP (Y/N)	Y
Year (Study Performed)	1991
Species	Rat
Strain	Sprague-Dawley CD, 41 days old at initiation of treatment
Route of administration	Oral gavage (syringe and dosing tube)
Duration of test	28 days of treatment and 14 day recovery period in the control and high dose satellite recovery groups
Doses/concentration levels	0, 100, 300 and 1000 mg/kg/day
Sex	Males and females
Exposure period	28-day treatment duration with a 14 day recovery
Frequency of treatment	7 days/week
Control group and treatment	5 rats/sex/group for each dose, and satellite recovery groups of 5 animals/sex for the control and 1000 mg/kg/day dose. Control group received daily doses of corn oil at 2.0 ml/kg, and treatment groups received the indicated dose of test material diluted in corn oil in a volume not to exceed 2.0 ml/kg
Post exposure observation period	14-days
Statistical methods	Body weight, food consumption, hematology and clinical chemistry parameters, organ weights and organ/body weight ratios were analyzed. Mean values of all dose groups were compared to control at each time interval. Tests included parametric ANOVA with a Dunnett's *post-hoc* test, non-parametric Kruskal-Wallis and Dunn's rank sum test, Bartlett's test for equal variances, and Student's *t*-test.
Remarks field for test conditions	Significant deviations from the OECD 407 test guidelines include: • A function observational battery for neurotoxicity was not performed since this test was not part of the OECD 407 guideline at the time the study was performed
Results	
Remarks	No NOAEL was assigned to this study. All animals survived throughout the study and physical examinations

were generally unremarkable. Test material administration produced alterations in the liver and kidneys of treated animals that were evident in the evaluation of organ weights as well as gross and microscopic pathological examinations.

Dose-related elevations in mean liver weights and/or liver/body weight ratios were seen at study termination in males at all dose levels and in females at the mid- and high-dose levels. Recovery was apparent during the two-week recovery period for the high-dose group. Gross post mortem examination of the liver revealed an accentuated lobular pattern in the mid- and high-dose females at termination of the dosing period, which resolved during the recovery period. Microscopic examination of liver revealed hepatocyte hypertrophy in all dose groups at the termination of treatment. This effect continued through the recovery period. The effect on the liver was consistent with the adaptive induction of hepatic metabolic mechanisms in response to a xenobiotic challenge.

Kidney alterations were seen only in males. Kidney weights and kidney/body weight ratios for high-dose males were significantly higher than control values at termination of dosing. These values were comparable following termination of the recovery period. Gross post mortem examination of the kidneys revealed pale or tan discoloration of increasing frequency with increased dose. Microscopic alterations consisted of increased incidences of globular casts and hyaline droplets in treated males. Hyaline droplets in the proximal tubules were seen at termination of dosing only, indicating that this change in renal morphology was reversible after cessation of test substance administration. The renal effects are consistent with previous reports in the scientific literature of male rat-specific hydrocarbon nephropathy. Evaluation of clinical chemistry and urinalysis studies revealed no evidence of renal or hepatic functional alterations, or any other signs of systemic effects due to the test material. Other minor effects of the test material consisted of a transient decrease in food consumption and body weight gain in the high-dose male group during the first week of study. A slight decrease in hemoglobin and hematocrit values was observed in the high-dose female group at termination that was found to be reversible during the 2-week recovery period.

Conclusions	Although renal and hepatic changes were evident at all dose levels (100, 300, and 1000 mg/kg/day), the renal changes are species-specific and the hepatic changes are probably adaptive in nature. Therefore, little subchronic toxicity was observed over the range of doses administered in this study.
Data Quality	Reliable without restriction (Klimisch Code)
References	This robust summary was prepared from an unpublished study by an individual member company of the HERTG (the underlying study contains confidential business information).
Other	Updated: 12-27-99